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Pancreatic carcinomas smaller than 3.0 cm: endosonography (EUS) in diagnosis, staging and prediction of resectability

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Background

The size of a pancreatic carcinoma determines prognosis and resection. The aim of this study was to review our clinical experience with endoscopic ultrasound (EUS) in diagnosing and staging pancreatic tumours <3.0 in diameter.

Methods

From February 1997 to October 2000 medical records and results of abdominal ultrasound (US), spiral computed tomography (CT) and EUS with fine-needle aspiration biopsy (FNA) were reviewed in 17 patients operated for histologically proven pancreatic adenocarcinoma measuring ≤3.0 cm in diameter. The mean age of the patients was 64 years (range 42–76 years).

Results

US identified a pancreatic lesion in 11/17 (65%) patients. Spiral CT showed a total of 16/17 (94%) patients with a lesion. EUS identified pancreatic tumour in all patients (100%), and tissue was obtained from 15/17 patients (88%). Mean tumour size was 2.5 cm (range 0.8–3.0 cm). EUS accuracy in evaluating the portal vessels was 78%, superior mesenteric artery 100%, tumour stage (T) 88%, isolated node stage (N) 65% and combined TN staging was 53%. Regarding resectability, EUS sensitivity was 88%, specificity 89%, negative predictive value 89%, positive predictive value 88% and accuracy 88%. Besides cytological material, EUS-FNA histological diagnosis was possible in 12/17 patients (71%). There was only one case of mild post-procedure acute pancreatitis.

Conclusion

EUS-FNA is safe and has high diagnostic (100%) and local staging (88%) accuracy in pancreatic cancers <3.0 cm in diameter.

Keywords

small pancreatic cancers, endoscopic ultrasound

Introduction

The diagnosis of small pancreatic cancer (SPC) is important in the prognosis of the disease [1]. Tumours <2.0 cm are frequently resectable and the 3-year survival rate is as high as 82%, but they are rarely diagnosed at such a small size. For tumours >2.0 cm the survival rate falls to 17% [1], but diagnosis and staging is still a clinical challenge with conventional imaging methods [2].

Endoscopic ultrasound (EUS) allows high-resolution pancreatic imaging and is considered the procedure of choice in the diagnosis of small tumours [3]. It has high sensitivity and specificity for tumours <1.0 cm, including insulinomas [4], and should be mandatory when conventional ultrasound (US), spiral computerised tomography (CT) or endoscopic retrograde cholangiopancreatography (ERCP) are inconclusive [3, 5]. It is not possible to differentiate tumours from inflammation by EUS [6]. In such cases, EUS-guided fine-needle aspiration (EUS-FNA) allows tissue sampling with cytological and histological diagnosis [7].

This study was a retrospective review of our experience with EUS-FNA in the diagnosis, staging and prediction of resectability for pancreatic cancers <3.0 cm in maximum dimension.

Patients and methods

Between February 1997 and October 2000, 763 EUS were performed on two endoscopy units. All procedures were performed with a Pentax sectorial scanning echoendoscope (FG 32-UA or FG 36-UX, Pentax Precision Instruments Corp., Orangeburg, NY, USA) and a Hitachi ultrasound unit (Mitsubishi, Conshockon,

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Table 1. *Overall clinical, image tests and operative staging in the 17 patients with pancreatic tumours <3.0 cm.*

Case	Age	Sex	US	CT	Size (cm)	Site	EUS TN	Surgery TN	EUS- FNA
1	68	M	C	C	0.8	H	T1N0	T1N0	MCA
2	62	F	−	−	1.8	H	T1N0	T1N1	Neg
3	46	M	+	+	2.8	H	T2N0	T4N0	Neg
4	42	M	+	+	3.0	H	T2N0	T2N0	Pos
5	67	M	−	ET	2.6	T	T2N0	T2N1	Pos
6	73	M	+	+	2.9	H	T2N1	T2N1	Pos
7	72	F	−	EB	2.5	B	T3N1	T3N1	Pos
8	67	F	+	+	3.0	H	T4N0	T4N0	Pos
9	57	F	−	EH	3.0	H	T4N1	T4N0	IN
10	75	F	−	+	2.6	H	T2N0	T4N0	Pos
11	65	F	−	EH	2.5	H	T4N0	T4N1	Pos
12	76	F	+	+	2.0	H	T4N0	T4N1	Pos
13	65	M	EH	EH	2.8	H	T4N0	T4N1	IN
14	55	F	MPDD	C	2.8	B	T4N1	T4N1	Pos
15	70	F	MPDD	EH	2.6	H	T4N1	T4N1	Pos
16	68	F	+	+	2.9	H	T4N1	T4N1	Pos
17	57	F	+	+	2.7	H	T4N1	T4N1	Pos

M, = male; F = female; C = cyst; − = normal test; + = mass or nodule; E = enlargement; H = pancreatic head; B = pancreatic body; T = pancreatic tail; MPDD = main pancreatic duct dilation; MCA = mucinous cystadenoma; IN = inadequate; Neg = negative for malignancy; Pos = positive for malignancy.

Philadelphia, USA) with frequencies of 5.0 and 7.5 MHz. Fine-needle aspirations were performed at the end of each procedure using the 19G GIP system (Medizintechnik GmBH, Grassau, Germany).

The head of the pancreas, portal system (portal and superior mesenteric vein), common bile duct, pancreatic duct, major papilla and right hepatic lobe were studied with the endoscope in the duodenum. The body and tail of the pancreas, splenic vein and left liver lobe were examined from the stomach. The tumours were classified according to the TNM classification. Tumours invading the portal system and/or superior mesenteric artery (irregularity of the vessel wall or invasion by tumour or thrombus) were considered non-resectable (graded as T4).

EUS was indicated to evaluate abnormal bilio-pancreatic findings seen on US, CT scan or ERCP in 359/763 patients (47%). EUS-FNA to rule out pancreatic tumours was performed in 132 patients (36.7%).

Seventeen patients (11 females, 64.7%) with small pancreatic cancers (maximum diameter $\leq$3.0 cm) seen on EUS were referred for operation and are reported in this study. The mean age of the patients was 63.8 years (range 42–76 years). All patients underwent US and CT scans before EUS-FNA. Surgical evaluation was considered the gold standard method for staging, and only operated patients in whom adenocarcinoma was confirmed by histology were included. Brazil has an open access system to endoscopy and echoendoscopy, so the primary physician and/or the surgeon were responsible for the decision to operate on a particular patient or not.

Sensitivity, specificity, positive and negative predictive values (PPV, NPV), accuracy and 95% confidence intervals were determined. The Q Cochran test was used to compare US, CT scan and EUS, with a p value <0.05 considered significant.

Results

Table 1 summarises overall data. Three tumours were <2.0 cm, 11 were between 2.1 and 2.9 cm and 3 were 3.0 cm in diameter. Mean diameter was 2.5 cm (range 0.8–3.0 cm). The tumour was located in the head of pancreas in 14 patients, in the body in 2 patients and in the tail in 1 patient.

US identified a pancreatic lesion in 11/17 (65%) patients: 7 pancreatic mass, 2 pancreatic duct dilation and one each pancreatic cyst and pancreatic head enlargement. CT scans showed lesions in 16/17 (94%) patients: 8 pancreatic masses, 6 pancreatic enlargements and 2 pancreatic cysts (Table 2).

EUS-FNA

We performed 37 needle passes in 17 tumours (mean 2.1 passes/tumour, range 1–4). Cytological examination was possible in 16/17 (94%) patients and histological analysis

Table 2. *Sensitivity of imaging tests for pancreatic cancers <3.0 cm in diameter according to the presence of any lesion on imaging tests.*

	Tumour size (cm)			
Imaging test	**≤2.0 (%)**	**2.1–2.9 (%)**	**3.0 (%)**	**Overall (%)**
US	2/3 (66.6)	7/11 (63.6)	2/3 (66.6)	64.7
CT	2/3 (66.6)	11/11 (100)	3/3 (100)	94.1
EUS	3/3 (100)	11/11 (100)	3/3 (100)	100.0
Total	3	11	3	17

in 14/17 (82%). A correct diagnosis of pancreatic cancer was obtained in 12/17 tumours (71%) based on EUS-FNA. If the two patients from whom adequate material was not obtained are excluded, sensitivity increases to 80% (12/15). EUS showed a hepatic nodule in one patient that was confirmed as a pancreatic adenocarcinoma metastasis by FNA. One patient developed mild acute pancreatitis after the procedure, and was admitted for 2 days.

Lymph node involvement (N1) was suspected in seven patients, and in each case EUS-FNA confirmed or excluded the cancer.

TN staging

In 15/17 (88%) patients EUS 'T' staging was confirmed during operation. Two patients were graded as T2 on EUS, whereas surgical staging revealed a T4 tumour. Surgical and/or histological staging confirmed the EUS 'N' staging in 11/17 (65%) patients (five N0, six N1). Five cases were staged as N0 by EUS but histology showed N1 tumours (understaging). The remaining case was overstaged by EUS. The correlation between surgical and EUS 'TN' staging was correct in 9/17 (53%) patients.

Vascular invasion

Tumour invasion of the portal venous system occurred in 9/17 (53%) patients, and EUS showed invasion in 7 of these (78%). Eight patients without portal system invasion were correctly diagnosed by EUS. The superior mesenteric artery was invaded in 3/17 (18%) patients, all diagnosed by EUS. In the 14 cases without mesenteric artery involvement, EUS showed one false positive result. Table 3 shows the results and statistical analysis.

Resectability

Tumour resection was possible in 8/17 (47%) patients (5 lesions in the head, 2 in the body and 1 in the tail) and it was considered to be complete in six. In two patients (one tumour in the head and one in the body) the resection was incomplete. EUS correctly diagnosed resectability in 7/8 (88%) patients. Of nine irresectable tumours, EUS correctly staged eight (all lesions in the head of pancreas).

Discussion

During EUS the whole pancreas can be examined in almost all patients, as gas and fat interference are eliminated [2]. EUS efficacy in the identification of small tumours has been compared with that of US and CT scans [2, 8].

CT scan involves administration of intravenous contrast and acquisition of thin cut images. When the whole gland is opacified, tumours <2.0 cm can be identified with an accuracy ranging between 90% and 100% [9]. CT scan accuracy to predict resectability is near 100%, whereas the irresectability rate is around 30% [10].

EUS-FNA should be indicated in cases where CT scan and US are inconclusive [5]. Parasher and Buthani performed EUS-FNA and found pancreatic cancer in 6/29 patients with non-specific pancreatic changes [5].

Pancreatic tumour diameter is an important prognostic

Table 3. *Results for vascular invasion and resectability as predicted by EUS-FNA.**

	Portal system invasion		SMA invasion		Resectability	
Parameter	**(%)**	**95% CI**	**(%)**	**95% CI**	**(%)**	**95% CI**
Sensitivity	78	40.2–96.1	100	31.0–100	88	46.7–99.3
Specificity	100	59.8–100	93	64.2–99.6	89	50.7–99.4
Positive predictive value	100	56.1–100	75	21.9–98.7	88	46.7–99.3
Negative predictive value	80	44.2–96.5	100	71.7–100	89	50.7–99.4
Accuracy	88	62.3–97.9	94	69.2–99.6	88	62.3–97.9

* Operative assessment was the final arbiter.

factor. Several years ago Tsuchiya and colleagues [11] showed a 5-year survival rate of 30% for patients with tumours <2.0 cm. In another series, patients with tumours <2.5 cm had a longer survival period than those with cancers >2.5 cm (25 vs 15 months) [12]. In a study conducted at the Mayo Clinic the authors have shown a survival rate of 20% after resection of tumours <2.0 cm, compared with 1% for tumours >3.0 cm [13].

EUS is a good method for identifying and staging small pancreatic cancers, defining those that are resectable [14, 15]. It also allows tissue sampling to confirm the presence of malignancy [7]. Studies have shown preoperative accuracy rates ranging from 78% to 94% for T staging [15–17] and from 64% to 82% for N staging [15, 17, 18].

CT scan has been compared with EUS in the identification and staging of pancreatic cancer. Legmann and associates [19] reported 90% accuracy for EUS in predicting resectability, a higher rate than for CT. Gress and co-workers [20] evaluated EUS and CT in PC staging, showing an accuracy of 93% in EUS prediction of resectability. The accuracy for T and N staging was 85% and 72% respectively.

Recent series have shown less encouraging results regarding EUS accuracy. A Japanese study reported accuracy of 64% and 50% for T and N staging [21]. In another study [22] of patients with T1 and T2 tumours, the accuracy for T and N staging was 69% and 54% overall and 61% and 78% for the more advanced (T3 and T4) lesions.

In view of published reports [22–25], we believe that the initial enthusiasm for EUS in pancreatic cancer staging should be redefined. Some details in these reports need to be clarified, notably the fact that negative margins in the resection specimen do not reflect the real stage of the disease. Lymph node involvement has been found even when no imaging method allowed its detection. Moreover, surgeons can overestimate vascular involvement at operation.

The low sensitivity in evaluating metastatic lymph nodes might be related to difficulties in identifying them. Peri-tumoral inflammation reduces specificity, as EUS may recognise inflammatory lymph nodes as mestastases [26].

In our study all procedures were performed with an electronic sectorial scanning echoendoscope. We consider it unnecessary to use a radial echoendoscope, as proposed by Chang and colleagues [7]. EUS-FNA (to differentiate benign from malignant lesions) has some advantages when compared with CT-FNA or US-FNA: shorter distance between the endoscope and the tumour, real-time control of the procedure and the use of Doppler to identify blood vessels, reducing the risk of bleeding [7, 27]. We were able to obtain adequate tissue samples with EUS-FNA in all except two patients.

We conclude that EUS-FNA should be performed in the diagnostic work up of pancreatic lesions <3.0 cm not confirmed by US and/or CT. The technique is safe and may supply tissue for histological confirmation of the malignancy (EUS-FNA). We also showed good results in T staging, vascular invasion and prediction of resectability.

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